2017

Patient characteristics associated with adherence of pulmonary nodule guidelines

BOSTON UNIVERSITY

SCHOOL OF PUBLIC HEALTH

Thesis

PATIENT CHARACTERISTICS ASSOCIATED WITH ADHERENCE OF PULMONARY NODULE GUIDELINES

by

JONATHAN M. IACCARINO

B.S., Georgetown University, 2006
M.D., Georgetown University, 2010

Presented in partial fulfillment of the

requirements for the degree of

Master of Science

2017

Approved by

First Reader

Jack A. Clark, Ph.D.
Professor of Health Law, Policy and Management

Second Reader

Renda S. Wiener, M.D., MPH
Associate Professor of Medicine
Boston University, School of Medicine

PATIENT CHARACTERISTICS ASSOCIATED WITH ADHERENCE

OF PULMONARY NODULE GUIDELINES

JONATHAN M. IACCARINO

ABSTRACT

Background: Pulmonary nodules are a frequent incidental finding on CT imaging and present a diagnostic challenge to clinicians, who must balance the risks of under-evaluation and over-evaluation. Determining why patients have delayed or no follow-up for incidentally found nodules is critical to optimizing pulmonary nodule outcomes and improving early detection of potential lung malignancy.

Methods: I performed a retrospective analysis of all patients found to have new pulmonary nodules on CT imaging at Boston University Medical Center between January 1, 2011 and June December 31, 2014. The primary outcome was rate of pulmonary nodule follow-up consistent with the 2005 Fleischner Society Guidelines. I assessed how various patient demographic and clinical factors were associated with whether timely follow-up occurred in order to identify potential characteristics that may contribute to non-guideline adherent evaluation.

Results: Among 3916 patients found to have a pulmonary nodule during the study period, 1152 patients met study criteria. In the study population, 613 patients (53.2%) had follow-up consistent with the 2005 Fleischner Society Guidelines. In bivariate analysis, increasing nodule size, white non-Hispanic race/ethnicity, and a co-diagnosis of

COPD were associated with guideline concordant follow-up. In multivariate analysis, patients with nodules measuring 7–8mm (OR 1.58, CI 1.06–2.37) and greater than 8mm (OR 1.63, CI 1.12–2.37) were more likely to have guideline concordant follow-up as were patients with a co-diagnosis of COPD (OR 2.00, CI 1.45–2.75). Hispanic patients were significantly less likely to have guideline concordant follow-up (OR 0.59, CI 0.36–0.97) compared to white non-Hispanics and uninsured patients were less likely to have guideline concordant follow-up (OR 0.56, CI 0.33–0.96) than patients with Medicare. Similar patterns were noted in analysis of nodules at highest risk of malignancy measuring 7mm or greater.

Conclusion: Overall, the rate of guideline concordant pulmonary nodule follow-up evaluation was found to be low. Guideline concordant follow-up was significantly associated with nodule size and presence of COPD, while delayed or absent follow-up was associated with Hispanic ethnicity and lack of insurance. While these factors may highlight potential targets for quality improvement, further research is needed to better understand the complexities in delivering guideline concordant care to patients in order to improve pulmonary nodule outcomes

Table of Contents

List of Tables

List of Figures

INTRODUCTION

Problem Statement

Despite advances in diagnostic methods and treatment, lung cancer continues to have a high mortality rate. Given rates of cure and survival are improved with early diagnosis, current strategies for reducing lung cancer mortality are aimed at early detection and intervention. Many lung cancers are detected at the earliest stage as a pulmonary nodule, a small growth in the lung seen on imaging measuring less than 3cm. Appropriate diagnosis and evaluation of pulmonary nodules to identify the subset that are malignant is essential to improving lung cancer outcomes. However, pulmonary nodules present a diagnostic dilemma for clinicians. Of the millions of nodules diagnosed yearly, the vast majority are benign and would require no further intervention. On the other hand, the minority of nodules that are malignant represent a potentially deadly diagnosis for which early intervention can be life-saving. To help clinicians efficiently and effectively manage nodules, clinical guidelines present a strategy for evaluation in an attempt to minimize over-evaluation of likely benign nodules and under-evaluation of likely malignant nodules. Currently, however, actual clinical practice strays widely from guideline-recommended pulmonary nodule care, increasing risks of patient harms from unnecessary procedures as well as missed opportunities for intervention of early malignancy, which may lead to a delay in diagnosis and treatment of cancer. Therefore, interventions to improve guideline concordance in the clinical setting need to be identified in order to optimize pulmonary

nodule evaluation and improve patient outcomes. There are multiple targets for potential optimization in the pulmonary nodule evaluation process, occurring at the patient, clinician, and healthcare system levels. While contributions from each of these three areas may improve guideline concordance, understanding potential patient characteristics that may increase risk of being lost to follow-up is a critical first step. This study will evaluate patient characteristics associated with guideline concordant pulmonary nodule follow-up to determine if and what disparities may exist. These findings will be used in a future intervention and implementation study to try to optimize pulmonary nodule follow-up.

Literature Review

Lung cancer: The leading cause of cancer death

Lung cancer is the leading cause of cancer death in both men and women, accounting for 28% of cancer deaths in men and 26% of cancer deaths in women.[1] While many cancer types have seen a significant improvement in 5-year survival rates over the past 25 years, there has been no change in survival rate for lung cancer with 5-year survival in 2009 estimated to be 14%, nearly identical to the estimated 12% rate in 1975.[1] Recent strategies for reducing lung cancer mortality has been multi-faceted with efforts aimed at both reducing risk factors for lung cancer and early detection. Risk factor reduction has mainly been through smoking cessation, with significant decreases in smoking rates with the advent of dedicated smoking cessation programs and

medications to aid in the quitting process.[2–8] Early detection has been attempted at several levels: lung cancer screening with yearly low-dose chest computed tomography (CT) scans,[9–15] utilization of biomarkers to determine patient risk,[16,17] and optimization of pulmonary nodule evaluation.[18,19]

The main theory behind early detection of lung cancer is that survival can be improved with identifying lung cancer at earlier and more treatable stages. This is the main support for both lung cancer screening with yearly CT imaging and biomarkers that might risk-stratify patients predisposed to developing lung malignancy. Early detection has been supported as a strategy for improving survival in lung cancer in several studies, but perhaps most notably in the National Lung Screening Trial.[15] However, there are potential problems that arise with the strategy of early detection, namely the risk of false positive results and the potential to identify and intervene upon disease that might have otherwise never caused morbidity or mortality (i.e. “overdiagnosis”). This is particularly of note given the experience with prostate cancer, in which early detection has not lead to improved mortality, resulting in major changes in the approach to prostate cancer screening.[20–23]

Optimization of pulmonary nodule management differs from the other strategies of early detection. While yearly low dose CT imaging and biomarkers can be used in screening asymptomatic patients for lung cancer, pulmonary nodule management

occurs in patients already determined to have an abnormality. These are patients found to have an incidental nodule on an imaging study that carries with it a potential risk of malignancy. This is in contrast to screening studies: while screening studies attempt to identify patients with an imaging abnormality, pulmonary nodule management requires evaluation of an abnormality already known to exist. However, false positives are still potentially problematic, given the vast majority of these nodules will be benign, and the risk for overdiagnoses remains an issue.

Pulmonary nodules: the key to early lung cancer detection

Pulmonary nodules are common findings on routine imaging of the chest, such as chest x-rays or CT scans. Pulmonary nodules have represented a diagnostic challenge for clinicians dating back to the discovery of the x-ray in 1897. The approach to evaluation and treatment of these findings were controversial in the early years of the x-ray. In 1936, Graham and Singer argued for surgical removal of all pulmonary nodules as the treatment modality of choice.[24] Similarly, Alexander in 1942 and Harrington in 1951 both described thoracotomy as the optimal method for diagnostic workup for a solitary pulmonary nodule.[25,26] However, over the next decade, it was recognized that a pulmonary nodule could represent a number of diseases, both malignant and benign, with significant difficulty differentiating between the potential diagnoses.[27–32] In 1956 and 1958, two different case series on pulmonary nodules attempted to identify patterns associated with increased likelihood of malignancy.[33,34] Their findings

suggested that there were perhaps characteristics of the nodule itself including its rate of growth that could indicate whether a nodule had malignant potential. The evaluation of pulmonary nodules with x-ray alone remained a suboptimal modality; although it was clear that surgical resection of all nodules was certainly unwarranted, as the large majority appeared to be benign.

The development of the CT scan in the early 1970s was a major advance in the identification, evaluation, and management of the pulmonary nodule. Soon after CT imaging started being utilized in clinical care, the increased sensitivity for identification of pulmonary nodules was apparent.[35,36] With an increased number of nodules to evaluate and greater detail in the modality of detection, researchers were better able to identify patterns in nodule appearance, including size, shape, and calcification pattern, as well as the rate of nodule growth associated with malignant vs. benign lesions.[37–40] However, the challenge of determining which nodules warranted additional follow-up and which could be observed remained and would continue to be a diagnostic dilemma for clinicians over the next several decades.

Since the early development of the CT scan, there have been significant improvements in the method and quality of CT imaging. This has led to an increased number of identified nodules given an even higher sensitivity and the increased utilization of CT imaging as a diagnostic modality for a variety of diseases. It is now estimated that

pulmonary nodules occur as an incidental finding in up to 39% of all CT scans performed.[41,42] This accounts for approximately 1.5 million nodules identified on a yearly basis.[43] Most of these nodules are benign findings, with 95% turning out to be inflammation, infection, scar tissue, or other non-malignant disease. While only 5% of these nodules turn out to be lung cancer, identifying potential cancer at this early stage would be a critical step in improving patient outcomes for lung cancer. As more nodules are identified, the importance of being able to distinguish between benign and early malignancy has been only magnified and remains, perhaps, one of the keys to improving lung cancer survival rates.

Guidelines for pulmonary nodule evaluation

The utilization of CT imaging in clinical practice increased the opportunity to study the natural history of pulmonary nodules and improved the ability to accurately describe changes in nodule size and character. Subsequently, studies were undertaken to better delineate nodules that appeared benign compared to those with malignant potential. In 1997, Swensen et al. performed a retrospective cohort study in order to derive a clinical prediction model to identify malignant nodules.[44] In their study, they determined several nodule characteristics (size, spiculation/shape, and location) that were associated with a higher risk of malignancy. Similarly, other studies evaluated the association between the rate of growth of a nodule and its malignancy risk.[45–49] Henschke et al. would take this a step further in 1999, identifying nodules with higher

risk features based on nodule size and characteristics and recommending follow-up CT imaging at 3, 6, 12, and 24-month intervals for these high-risk nodules.[50] While their study presented a potential strategy for nodule evaluation, they recognized a high false positive rate with this approach. Additional studies then looked to examine small, lower risk nodules to determine their optimal follow-up interval and try to limit the risk of false positive CT findings.[51,52] These studies were able to identify an approximate cutoff value of 4mm, below which it seemed the risk of malignancy was extraordinarily low (<1%) and limited, if any, follow-up was needed.

Simultaneous to these studies assessing malignancy risk based on nodule size and characteristics, other approaches attempted to identify high-risk patients that may require closer follow-up. It had been known for some time that the risk for developing lung cancer in smokers was significantly higher than in nonsmokers. This was outlined in the 1982 report of the Surgeon General in which smokers had a 10–15 times greater risk of lung cancer than nonsmokers.[53] However, family history of lung cancer and other exposures, such as asbestos, were newly identified risk factors that needed to be considered.[54,55] In these higher risk patients (smoking history, family history, asbestos exposure), the risk of an incidentally found nodule being malignant would be higher than their lower risk counterparts based on their higher baseline lung cancer risk. How to best integrate these findings with those focused on nodule characteristics remained unclear.

In response to the difficulty clinicians faced in their approach to pulmonary nodule evaluation, medical societies sought to compile guidelines based on the available evidence to aid clinicians in their decision-making process. One of the first and most popular guidelines was set forth by the Fleischner Society in 2005.[56] These guidelines used the findings of the prior studies looking at nodule size, growth rate, imaging characteristics, and patient risk factors to formulate recommendations for the optimal interval for follow-up imaging. The guidelines were organized into categories based on patient risk (low or high risk) as well as nodule size, with the recommended follow-up interval increasing with increased risk as well as with increase in nodule size (Figure 1). Other societies would also produce similar recommendations for how to best manage pulmonary nodules,[57,58] but the Fleischner Society guidelines would become one of the more commonly utilized guidelines based in part on their relative simplicity.

Figure 1: Fleischner Society 2005 recommendations for management of pulmonary nodules.[56]

Nodule Size (mm)*	Low-Risk Patient†	High-Risk Patient‡
≤4	No follow-up needed§	Follow-up CT at 12 mo; if unchanged, no further follow-up‖
>4–6	Follow-up CT at 12 mo; if unchanged, no further follow-up‖	Initial follow-up CT at 6–12 mo then at 18–24 mo if no change‖
>6–8	Initial follow-up CT at 6–12 mo then at 18–24 mo if no change	Initial follow-up CT at 3–6 mo then at 9–12 and 24 mo if no change
>8	Follow-up CT at around 3, 9, and 24 mo, dynamic contrast-enhanced CT, PET, and/or biopsy	Same as for low-risk patient

The algorithm recommended by the Fleischner Society, in addition to other medical societies producing guidelines, was a critical step forward in trying to optimize the

management of pulmonary nodules. However, there has remained significant variation in clinical practice and deviations from the recommendations provided by medical societies. Variation in clinical practice has been observed both on a geographic level as well as at the clinician level with variation noted among medical specialties. Multiple studies have assessed compliance with the Fleischner Society guidelines, in particular, looking at how frequently patients receive the ideal follow-up defined by prior evidence. One such study performed in a clinic dedicated to pulmonary nodule evaluation and follow-up found a guideline compliance rate of only 55%.[59] Other studies involving pulmonologists across the country have found similarly poor guideline compliance, with rates as low as 48% and some amount of geographic variation noted.[60,61] Amongst radiologists, who are responsible for interpreting CT scans and making recommendations based on the results, there is also notable deviation from guideline recommendations. One study showed adherence to the Fleischner Society guidelines among 834 radiologists to be 58.8%.[62] Another study surveying members of the Society of Thoracic Radiology utilizing clinical vignettes found 27% of radiologists made recommendations consistent with the Fleischner Society guidelines.[63]

The Fleischner Society guidelines are not the only guidelines that have been difficult to implement in clinical practice. A more recent guideline from the American College of Chest Physicians in 2013 outlines in more detail the recommended approach to the newly discovered solitary pulmonary nodule.[64] However, a study of community

pulmonologists found these guidelines to be poorly followed in clinical practice, with clinicians not appropriately discriminating in their management of low, intermediate, and high-risk nodules.[65] A separate study found this discordance from guideline recommendations persisted even when clinicians accurately predicted malignancy risk.[66] While there are numerous potential obstacles to implementation of pulmonary nodule guidelines, these studies seem to suggest clinicians' ability to perceive malignancy risk does not correlate with appropriate nodule management based upon guideline recommendations.

Clinical importance of pulmonary nodule guidelines

Deviation from guideline-recommended pulmonary nodule care is an example of the challenge of inducing clinicians to adopt and incorporate guidelines in their treatment of patients. When clinicians act in accordance with guideline recommendations, patient outcomes are theoretically optimized. In contrast, when clinicians act discordant to clinical guidelines, there may be significant risk of patient harm. With pulmonary nodules, guideline discordance may occur in the form of either under-evaluation (less aggressive testing of malignant nodules than guidelines recommend) or over-evaluation (overaggressive testing of benign nodules). Given the high mortality associated with lung cancer, missing the opportunity to intervene early on a nodule that turns out to be cancer could be devastating. If a pulmonary nodule were malignant, it more than likely would represent stage IA lung cancer, a potentially curable stage with surgical resection

that has a 5-year survival rate of 60%.[67,68] With every increase in cancer stage, 5-year mortality declines by 5–10% through stage IV cancer with a 1% 5-year survival,[1,69] stressing the potential impact early intervention may have on improving patient survival and outcomes.

Over-evaluation of pulmonary nodules also presents potential patient harms. Given that the large majority of nodules are benign, there is a relatively higher likelihood of subjecting patients to unnecessary interventions. Performing unnecessary follow-up CT scans increases a patient's radiation exposure and also increases the risk of other benign incidental findings that could require additional workup and evaluation. Additionally, a patient may be subjected to medical procedures including biopsies and potential surgery that could have significant clinical complications and morbidity.[70,71] There can also be notable mental health impact on patients, as the diagnosis of a pulmonary nodule has been shown to cause increased anxiety and emotional distress that can last for months to years.[71–74] Subjecting a patient to unnecessary follow-up testing may only serve to increase their anxiety and mental stress regarding the diagnosis. Over-evaluation of nodules may also have important implications on healthcare cost. With a pulmonary nodule evaluation estimated to cost approximately $50,000 per occurrence, performing unnecessary evaluations could lead to financial burden for both the patient and the healthcare system.[75]

The Fleischner Society guidelines were based on analysis of the available evidence and balanced the risks of under- and over-evaluation to try to optimize patient outcomes. While the absence of high-quality evidence comparing nodule evaluation strategies makes the "ideal" pulmonary nodule management unknown, the Fleischner Society guidelines provide an algorithm to assist clinicians in minimizing over- and under evaluation of pulmonary nodules in an attempt to optimize patient outcomes. These guidelines have ultimately been widely accepted as the standard of care for pulmonary nodule evaluation.

Lung cancer screening: raising the stakes

While the Fleischner Society guidelines were intended for aiding clinicians in managing incidentally found pulmonary nodules, recent recommendations for lung cancer screening have created another use for the guidelines. In 2013, the National Lung Screening Trial (NLST) demonstrated a reduction in lung cancer mortality by 20% with annual screening of high risk patients with low dose CT scans of the chest.[15] In their study, they performed yearly CT scans in smokers between the ages of 55 and 74. Based on the Fleischner Society guidelines, any pulmonary nodule that was over 4mm was considered a positive screen and was evaluated with additional CT imaging, or PET scan, biopsy, or surgical resection for higher risk nodules. However, the criteria used to determine the appropriate type of evaluation and time interval was not specified in the study, instead allowing trial radiologists to develop their own diagnostic follow-up

recommendations. Given a total false positive rate of 23% found in the NLST (and an even higher rate found in the real world setting[76]), there is potential for significant patient harm if nodules found during screening are not managed appropriately.

Without set criteria for managing nodules found during lung cancer screening, it is unclear what approach will allow clinicians in the real world to achieve the 20% reduction in lung cancer mortality seen in the NLST. In setting up lung cancer screening programs, guidelines recommend and the Center for Medicare and Medicaid Services (CMS) requires utilization of an algorithm, such as the Fleischner Society guidelines, for pulmonary nodule evaluation.[77–79]. With multiple societies including CMS now recommending annual CT scans for lung cancer screening,[11–14] it is expected that many more nodules will be found in these higher risk individuals. This will only magnify the need for guideline adherence, with the risks of under- and over-evaluation being raised even further.

Potential for disparities in pulmonary nodule evaluation

In order to improve the low rates of concordance with pulmonary nodule guidelines, it is important to first identify the reasons why some patients do not receive guideline-recommended care. It is particularly important to identify whether disparities exist between certain patient groups. Prior literature about other clinical conditions has documented poor guideline adherence particularly in patients of minority race, ethnicity,

and socioeconomic status. For instance, a study of diabetes care across the United States found lower rates of adequate diabetes and cholesterol control in blacks and Hispanics when compared to whites.[80] Similarly, a study of guideline adherence in asthma found patients without insurance were less likely to have recommended chronic asthma care compared to patients with public or private insurance.[81] Disparities in guideline-recommended care has been well documented in management of many other chronic diseases, including osteoporosis, human immunodeficiency virus, and congestive heart failure, among many others.[82–84]

Disparities have also been identified in preventive medicine, where clinicians aim to keep health patients from developing disease, and in disease screening aimed to identify illness at an early stage. A large study evaluating preventive medicine in cardiovascular care found lower rates of guideline-recommended blood pressure and cholesterol control in minority groups compared to whites as well as in women compared to men.[85] Racial and ethnic disparities have also been identified in diabetes screening, depression screening and diagnosis, and hepatitis B and C screening.[86–88] While disparities have not been yet well examined in pulmonary nodule evaluation itself, there have been notable disparities in cancer screening and in treatment of lung cancer. For instance, it has been well documented that lung cancer mortality outcomes are worse in minority groups and under and uninsured patients, with these groups presenting with more advanced disease and receiving less frequent guideline-

recommended cancer treatment than white and insured patients, respectively.[89–91] Studies have also found that minority patients may be less receptive to lung cancer screening due to fatalistic beliefs, suggesting cultural factors have the potential to impact lung cancer outcomes.[92,93]

With disparities in many other areas of preventive, diagnostic, and therapeutic medical management, it is likely that similar disparities exist in the evaluation of incidentally found pulmonary nodules. One method to combat these disparities in care is the development and implementation of clinical guidelines. Guidelines aim to provide a framework or algorithm for clinicians to follow and are particularly useful in times of clinical uncertainty. Given that pulmonary nodule guidelines help to "level the playing field" in various clinical scenarios by providing clarity in medical decision-making, it is important to determine 1) whether guidelines are being followed consistently and 2) if guideline adherence varies by patient characteristics (race/ethnicity, insurance status, etc.). Determining how guidelines are followed in the real-world setting will inform future studies in how to best implement practice changes to optimize pulmonary nodule evaluation and outcomes.

Conceptual Model

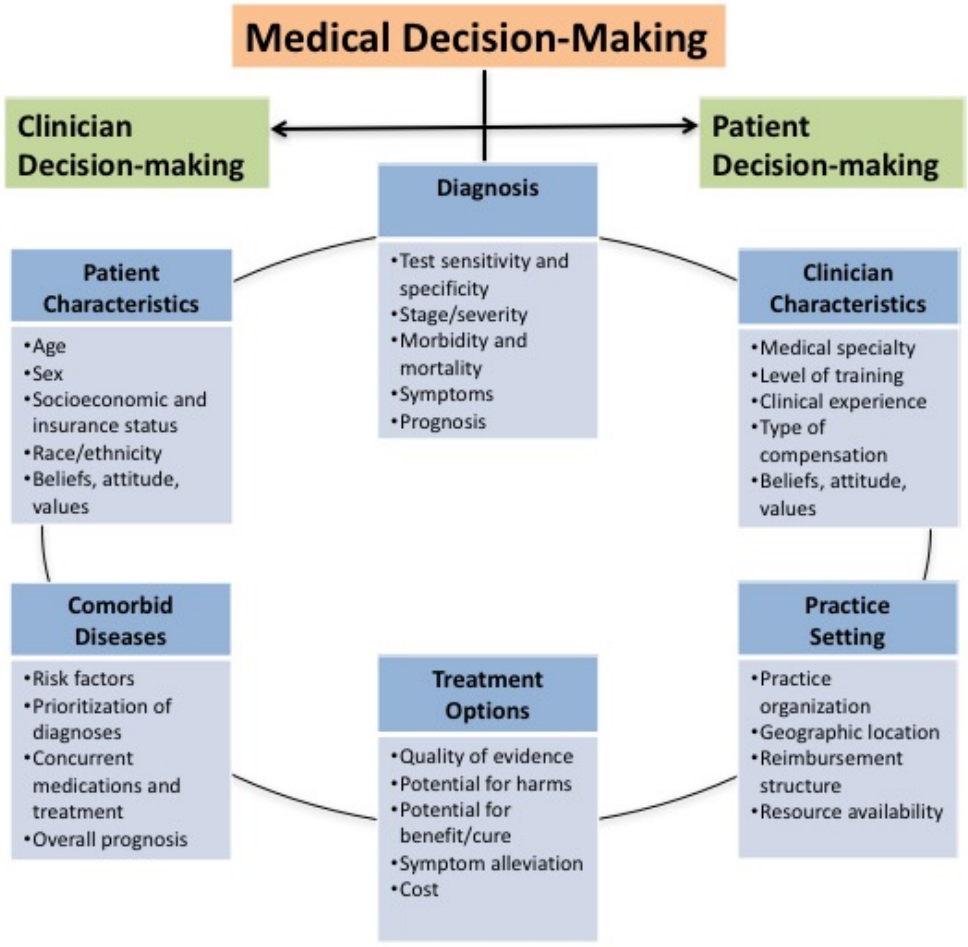
Whether a patient receives guideline-recommended pulmonary nodule evaluation is dependent upon a decision-making process rooted in a complex interrelationship

between patient, clinician, and the larger healthcare system. This decision-making process is ultimately comprised of both clinician and patient decision-making, as well as the interaction between the two parties (Figure 2). Within the decision-making process, multiple factors affect the decision-making process that occurs among and between patient and clinician. Some of these factors consist of the traditional clinical criteria that are based upon scientific evidence that provide data on various diagnostic tests, treatment options, and natural history of the disease of interest. Making a clinical decision requires, in part, the weighing of the risks and benefits of a proposed diagnostic study or intervention, taking into account the factors influencing these categories.

Other factors that affect decision-making are, perhaps, more complex. Patient characteristics, consisting of demographics (i.e. age, sex, race, socioeconomic status) and less easily defined characteristics (i.e. patient beliefs, fears, attitudes, and values) of course affect patient decision-making, but also may influence how the clinician perceives the patient.[94,95] Some of these characteristics may have direct clinical relevance, while others may be more be subliminal in how they influence clinician perceptions of patients' health. Similarly, clinician characteristics are made up of well-defined attributes, such as medical specialty or level of training, but also include factors such as clinical experience, values, and attitudes.[94,95] These factors may influence clinician decision, but also may affect patient perception of their clinician and how the patient interacts with the clinician in the decision-making process. Finally, there are

features of the practice setting that may influence how clinicians and patients make medical decisions. Characteristics such as the type of practice, geographic location, reimbursement structure, local culture and practice patterns, and availability of resources may be considerations for why a patient does or does not receive a certain diagnostic test or therapeutic intervention.[94,95]

Figure 2: Medical and non-medical factors influencing decision-making in pulmonary nodule evaluation (adapted from McKinlay et al.,[95] Charles et al.,[96] and Hajjaj et al.[94])



My study on pulmonary nodule evaluation will draw on this conceptual model (figure 2) to explore disparities among patients in guideline concordant pulmonary nodule evaluation. From this model, I propose three likely potential explanations that could account for the variation seen in guideline concordant pulmonary nodule evaluation: 1) Patients are unable or unwilling to undergo the follow-up evaluation recommended by their clinician; 2) Clinicians are unable or unwilling to implement guideline recommendations in real world practice; or 3) There is an insufficient availability of resources and processes of care at the healthcare system level to accommodate the required follow-up recommended in the guidelines. This study will take the first step in exploring the first of these explanations by evaluating patient factors associated with guideline adherence and nonadherence. This will serve to identify potential patient-level barriers to pulmonary nodule evaluation. With prior studies focusing at the clinician and healthcare system levels,[60,62,63,65,66,97–100] few studies have evaluated barriers to nodule guideline adherence at the patient level. Patient characteristics may impact patient knowledge, attitudes, and behavior related to being able to adhere to guideline recommendations.[101–103] Additionally, patient characteristics may also influence whether a clinician orders the appropriate test in the first place, as factors such as insurance status or patient values may influence how and when evaluations are performed. Predisposing characteristics, such as age, marital status, race/ethnicity, primary language, economic status, and education level are all potential influences on a patient's perceived need for care as well as clinician's perceptions of the patient's need

for care and could affect whether a patient ultimately receives the recommended follow-up. Determining which of these factors are associated with guideline- concordant and guideline-discordant pulmonary nodule evaluation will provide critical data to better understand medical decision-making in pulmonary nodule management.

Summary

The main goal of my study is to determine which patient characteristics are associated with pulmonary nodule evaluation guideline non-adherence. Identifying potential disparities in pulmonary nodule evaluation will provide valuable information to better understand which patients are at greatest risk of being lost to follow-up. My study plans to analyze the association of patient factors such as age, gender, marital status, race/ethnicity, primary language, economic status, and education level with pulmonary nodule guideline non-adherence. I will be evaluating all patients at Boston Medical Center who were found to have a pulmonary nodule between 2011 and 2014 (end date selected to allow at least two years of follow-up from the time of diagnosis). I will be determining which patients received appropriate follow-up based on the 2005 Fleischner Society guidelines. For this study, I will focus on pulmonary nodule follow-up that is at least as aggressive as recommended by the Fleischner Society guidelines. While over-evaluation certainly could lead to patient harm, there are potential clinical reasons for a patient to have follow-up sooner than recommended that are valid and reasonable. Moreover, missing a cancer, rather than harms of overtesting, is typically

the greatest concern of patients, clinicians, and healthcare systems, thus making it more pressing to identify (and ultimately to prevent) cases of under-evaluation than over-evaluation.[98,100,104] I will be comparing the patient characteristics of these two groups to try to identify associations with receipt of care that deviates from the guidelines. These data will be used to try to predict which patients are at highest risk of having poor pulmonary nodule follow-up and provide the basis for a future study utilizing patient navigation for these at-risk groups to improve pulmonary nodule outcomes. This may also generate hypotheses for potential intervention targets in other clinical settings on a more global level.

Research Questions

- What is the rate of pulmonary nodule follow-up at least as aggressive as recommended by Fleischner Society pulmonary nodule guidelines among the patients at Boston Medical Center?

  Hypothesis: Less than 50% of patients at BMC will have follow-up evaluation at least as aggressive as the Fleischner guidelines.

- Which patient characteristics are associated with lower rates of guideline-recommended pulmonary nodule follow-up?

  Hypothesis: Gender, marital status, economic status, and education level will be associated with rates of guideline-recommended pulmonary nodule follow-up.

Male gender, single marital status, lower economic status, and lower education level will have lower rates of guideline concordant pulmonary nodule follow-up.

Specific Aims

Aim 1: Determine the rate of concordance with the 2005 Fleischner Society pulmonary nodule guidelines (the accepted standard of care) at Boston Medical Center.

Aim 2: Determine which patient characteristics are associated with lower rates of guideline concordant pulmonary nodule follow-up.

METHODS

Data collection

Patients with new pulmonary nodules between 2011 and 2014 at Boston Medical Center (BMC) were identified using a database maintained by the radiology department. This database included patient identifiers, date of imaging study, size of pulmonary nodule identified, and recommendations for nodule follow-up. This was a clinical database that had been established the year prior as part of a quality improvement project to improve pulmonary nodule follow-up at BMC. Initially, all information used in this database was to be used for this study. However, while performing random chart review on 500 patients in the database to verify data integrity, numerous errors were found in the recording of nodule size and follow-up recommendations. Consequently, the only data used from this database were patient medical record numbers that indicated a new diagnosis of a pulmonary nodule during the study period of interest. We used this information to assemble a cohort of patients with newly diagnosed pulmonary nodules.

We then obtained data about patient characteristics, imaging study, and nodule characteristics for patients in our cohort from the BMC Clinical Data Warehouse (CDW). These data included patient demographics, primary language, insurance status, smoking history, education level, radiology report from imaging study of interest, patient comorbidities (based on ICD-9 codes), zip code, and subsequent chest CT occurring after

the initial pulmonary nodule diagnosis. Patient zip code was used to estimate median income based on data from the U.S. Census from 2011–2015.[105] Pulmonary nodule size was obtained from the radiology report as well as through chart review. Patient data were verified and missing data were supplemented using chart review.

Inclusion and Exclusion Criteria

All adult patients who were diagnosed with a new pulmonary nodule between 2011 and 2014 at BMC were included in this study. As a level 1 trauma center and tertiary care center, BMC sees a wide array of patients who receive their primary medical care across the country. This meant there was a chance that a patient found to have a pulmonary nodule at BMC may subsequently have their follow-up care at another institution. To assure that all follow-up data for patients would be available, I included only patients who had an office visit in a primary care clinic (internal medicine, family medicine, or geriatrics) or in pulmonary clinic at BMC in the year prior to or year following the diagnosis of their pulmonary nodule.

Patients were excluded from the study if their pulmonary nodule was greater than 3cm, if the nodule had been previously detected prior to the study period, or if they died prior to the recommended follow-up period based on the 2005 Fleischner Society Guidelines. Additionally, patients were excluded if they had a pulmonary nodule that did not require follow-up. Based on Fleischner guidelines, nonsmokers with a nodule of

4mm or less in diameter do not require follow-up and therefore were excluded. Finally, patients initially included who were found to not actually have a nodule on imaging or who had a nodule with no size reported were also excluded.

Primary and secondary outcomes

The primary outcome of this study was the proportion of patients who received pulmonary nodule evaluation consistent with the 2005 Fleischner Society guidelines among all patients in the cohort. Evaluation was dichotomized as guideline concordant (at least as aggressive as recommended by the guidelines) or guideline non-concordant (under-evaluation) based on comparison of the expected follow-up time period and the actual follow-up occurrence. The recommended pulmonary nodule follow-up dates were determined based on the Fleischner Society guidelines[56] using patient smoking history and nodule size. When the recommended follow-up consisted of a date range, the longer period in the range was used for a follow-up period (i.e., 6 months if the follow-up recommendation was 3 to 6 months). Follow-up evaluation consisted of either a chest CT, PET scan, bronchoscopy, or biopsy occurring within 30 days of the recommended period. Due to the nature of the data, it was not possible to determine if a repeat CT scan was obtained prior to the recommended date for a different clinical reason, thereby making it challenging to determine if patients are receiving pulmonary nodule follow-up more aggressive than recommend. Additionally, as previously stated, missing the opportunity to intervene early on malignancy is typically the greatest

concern of patients, clinicians, and healthcare systems.[98,100,104] Therefore, a follow-up study occurring prior to the recommended time frame was still considered in concordance with the guidelines in this study. The main secondary outcome in this study was any pulmonary nodule follow-up, defined as a patient receiving follow-up evaluation at any time during the study period.

Statistical Analysis

Guideline concordance was calculated by measuring the proportion of patients receiving follow-up prior to 30 days beyond guideline-recommended time period. Chi-squared and student t-tests were used, as appropriate to evaluate associations between patient characteristics and guideline concordant pulmonary nodule follow-up. All tests for significance were two tailed. The Kruskal-Wallis test was used to compare median income between groups. Income was estimated based upon zip code data obtained from United States Census data. Variables believed to be potential confounders (age, gender, race/ethnicity, insurance status, education level, smoking history, and median income) as well as those strongly associated with guideline concordant follow-up in binary analysis were included in a multivariable logistic regression model, with the dichotomous outcome of guideline concordant follow-up (yes/no) as the dependent variable. Odds ratios were calculated and reported with a 95% confidence interval.

In secondary analyses, I also assessed whether patients had follow-up for a newly diagnosed pulmonary nodule at any point during the study period. The statistical approach was the same except for using any follow-up as the dependent dichotomized variable. Additionally, I also evaluated patients with nodules of 7mm or greater using the same approach to determine differences in patients receiving guideline concordant follow-up compared with delayed or no follow-up for nodules at high risk of being malignant.

RESULTS

Of 3916 patients diagnosed with a pulmonary nodule between 2011 and 2014, 1152 patients were evaluated after applying the inclusion and exclusion criteria (Figure 3). Included patients in this study represented the overall demographic of patients who receive their care at BMC, with a large proportion of minorities, large number of uninsured and Medicaid patients, and low education level (Table 1).

Figure 3: Patients with a pulmonary nodule diagnosis during the study time period who were excluded and included from analyses.

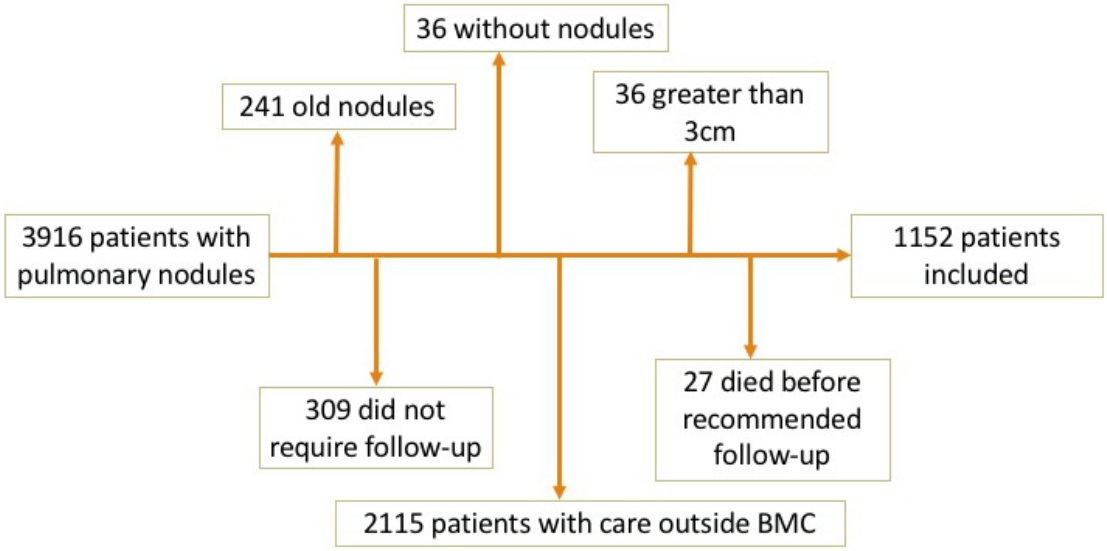


Table 1: Patient characteristics of all included patients.

Patient characteristic	**All included participants (n=1152)**
Age [mean (SD)]	60.5 (13.4)
Male sex	48.0%
Ethnicity	
White Non-Hispanic	36.9%
Black Non-Hispanic	45.3%
Hispanic/Latino	11.4%
Other	6.4%
English as primary language	78.4%
Insurance	
Medicare	38.0%
Medicaid	32.6%
Private	21.4%
Uninsured	8.0%
Current or former smoker	73.4%
Marital Status	
Single	40.6%
Married	33.7%
Other	25.7%
Education level	
Less than high school	14.9%
High School	67.7%
College or advanced degree	18.2%
BMI [mean (SD)]	29.0 kg/m^2 (8.4 kg/m^2)
Income [median (IQR)]	$52,122 ($25,785)

Of the 1152 patients evaluated in this study, 613 (53.2%) received follow-up within the time frame recommended by Fleischner Society guidelines. Of the 539 patients receiving guideline non-concordant follow-up, 307 (57.0%) had no follow-up evaluation at any point during the study period. In binary analysis, increasing nodule size (p=0.05), white non-Hispanic race/ethnicity (p=0.04), and a concurrent diagnosis of COPD were significantly associated with having guideline concordant follow-up (Table 2). While

insurance status did not reach statistical significance in this analysis, point estimates suggest a higher percentage of uninsured patients in the guideline non-concordant group (9.8%) compared to the guideline concordant group (6.3%).

Table 2: Comparison in characteristics of patients receiving guideline concordant pulmonary nodule follow-up and patients receiving non-concordant follow-up. Differences found to be statistically significant at a significance value of 0.05 are highlighted in bold.

Patient characteristic	**Guideline concordant (n=613)**	**Guideline non-concordant (n=539)**	**p-value**
Age at scan [mean (SD)]	60.6 (12.3)	60.4 (14.5)	0.77
Male gender	296 (48.3%)	257 (47.7%)	0.84
Ethnicity			**0.04**
Black non-Hispanic	**260 (43.1%)**	**252 (47.7%)**	
White non-Hispanic	**242 (40.1%)**	**175 (33.1%)**	
Hispanic/Latino	**59 (9.8%)**	**70 (13.3%)**	
Other	**42 (7.0%)**	**31 (5.9%)**	
English as primary language	488 (79.7%)	413 (76.8%)	0.22
Insurance			0.13
Medicare	245 (40.0%)	193 (35.8%)	
Medicaid	198 (32.3%)	177 (32.9%)	
Private	131 (21.4%)	116 (21.5%)	
Uninsured	39 (6.3%)	53 (9.8%)	
Current or former smoker	450 (73.4%)	396 (73.5%)	0.98
Marital Status			0.21
Single	235 (38.3%)	233 (43.2%)	
Married	211 (34.4%)	177 (32.8%)	
Other	167 (27.2%)	129 (23.9%)	
Education level			0.24
8^{th} grade or less	85 (14.5%)	78 (15.4%)	
High School	406 (69.1%)	328 (64.6%)	
College/professional degree	97 (16.5%)	102 (20.1%)	
BMI [mean (SD)]	28.7 kg/m^2 (7.1 kg/m^2)	29.4 kg/m^2 (9.8 kg/m^2)	0.20
Income [median (IQR)]	$52,122	$54,883	0.69

Nodule size			**0.05**
<= 4mm	**192 (31.3%)**	**208 (38.6%)**	
5–6mm	**191 (31.2%)**	**164 (30.4%)**	
7–8mm	**101 (16.5%)**	**71 (13.2%)**	
>8	**129 (21%)**	**96 (17.8%)**	
History of COPD	**173 (28.2%)**	**99 (18.4%)**	**<0.01**
History of diabetes	175 (28.6%)	136 (25.2%)	0.21
History of chronic renal disease	67 (10.9%)	53 (9.8%)	0.54

In multivariable logistic regression analysis (Table 3), Hispanic patients were found to have a significantly lower rate of guideline concordant follow-up compared to white non-Hispanics (OR 0.59, 95% CI 0.36-0.97). Additionally, uninsured patients were less likely to have guideline concordant follow-up compared to patients with Medicare. Similar to the pattern seen in binary analysis, there is an increasing likelihood of guideline concordant follow-up with increasing nodule size. Finally, patients with COPD were found to have twice the odds of having guideline concordant follow-up compared to those without COPD (OR 2.00, 95% CI 1.45–2.75).

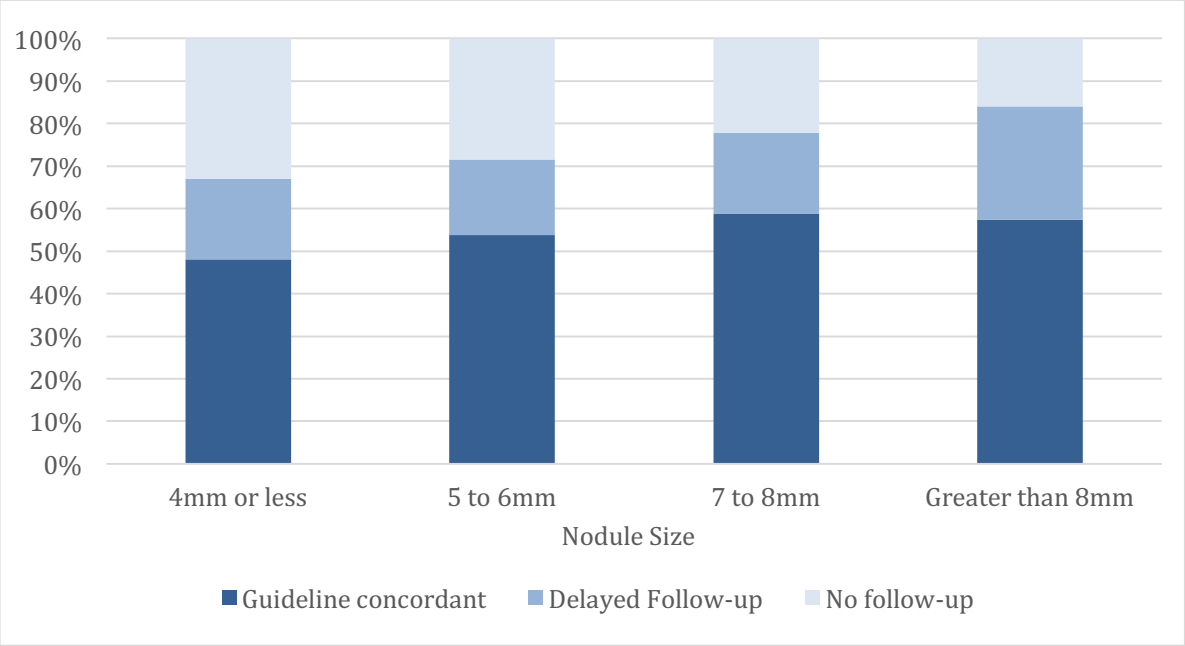
Table 3: Multivariable logistic regression analysis comparing patients with guideline concordant follow-up to guideline non-concordant follow-up. Characteristics reaching statistical significance highlighted in bold.

Patient characteristic	Odds ratio (95% CI)	p-value
Race/Ethnicity		
White Non-Hispanic	Ref	
Black Non-Hispanic	0.80 (0.59–1.08)	0.14
Hispanic	**0.59 (0.36–0.97)**	**0.04**
Other	1.12 (0.61–2.07)	0.72
Insurance		
Medicare	Ref	
Medicaid	0.87 (0.62–1.20)	0.39
Commercial/Private	0.88 (0.62–1.24)	0.46
Uninsured	**0.56 (0.33–0.96)**	**0.04**
Nodule Size		
4mm or less	Ref	
5 to 6mm	1.36 (0.98–1.88)	0.07
7 to 8mm	**1.58 (1.06–2.37)**	**0.03**
Greater than 8mm	**1.63 (1.12–2.37)**	**0.01**
History of COPD	**2.00 (1.45–2.75)**	**<0.01**

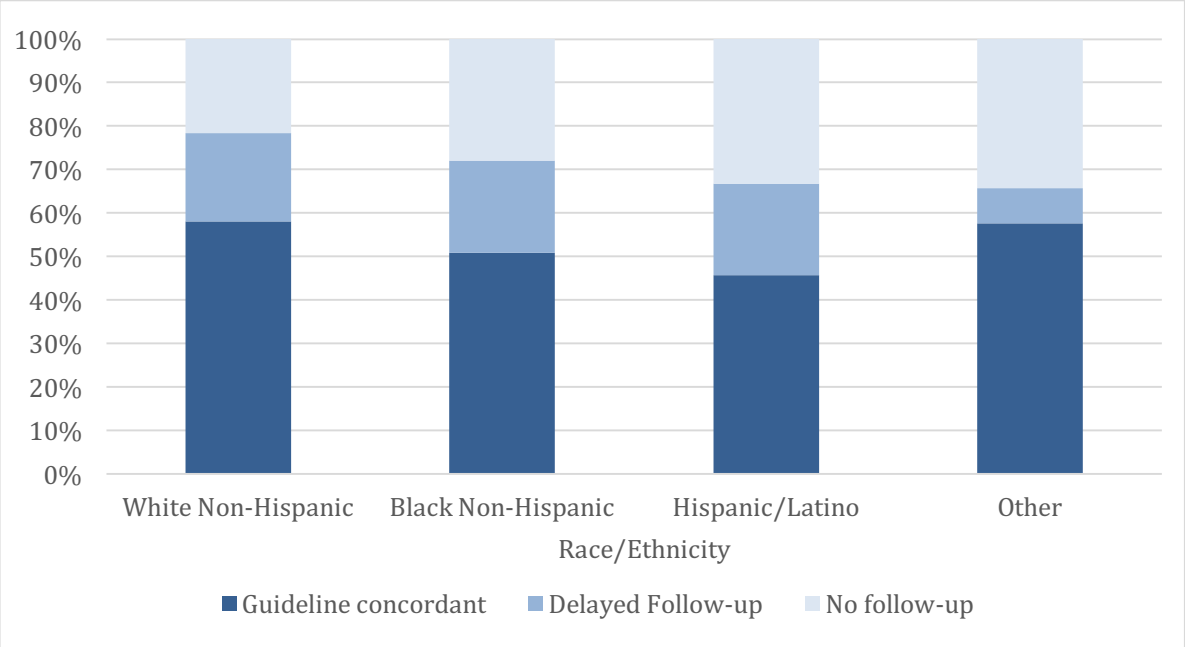
Similar patterns were observed when evaluating which patients had any follow-up at any time during the study period (Figure 4). With increasing nodule size, there was an increasing rate of not only guideline concordant follow-up, but overall follow-up as well (Figure 4a). While only 15% of patients with a nodule greater than 8mm had no follow-up at any time during the study period, nearly 35% of patients with a nodule 4mm or less had no follow-up. When categorizing patients by race/ethnicity (Figure 4b), Hispanic/Latino patients had not only less guideline concordant follow-up compared to whites (45.7% vs. 58.0%, p=0.01), but also higher rates of having no follow-up (33.3% vs. 21.6%, p<0.01). Patient insurance status also was associated having no follow-up (33.3%

Figure 4: Rates of guideline concordant follow-up, delayed follow-up, and no follow-up based on (a) nodule size, (b) patient race/ethnicity, and (c) patient insurance status.

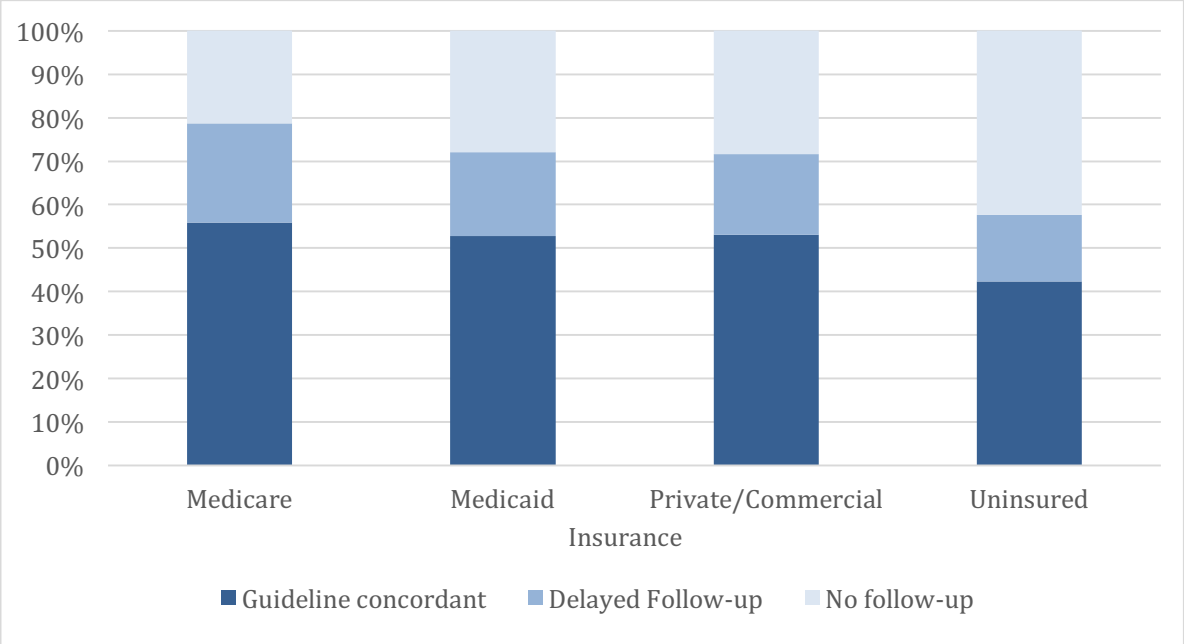
(a)



(b)



(c)



vs. 21.6%, p<0.01). Patient insurance status also was associated with both guideline concordant follow-up and any follow-up (Figure 4c). Uninsured patients had significantly less guideline concordant follow-up compared to Medicare patients (42.4% vs. 55.9%, p=0.02) as well as higher rates of having no follow-up during the study period (42.4% vs. 21.2%, p<0.01).

In the binary analysis of patients with larger nodules (Table 4), measuring 7mm or greater, patients with a concurrent diagnosis of COPD were more likely to have guideline concordant follow-up than those without COPD (p<0.01). In multivariate analysis (Table 5), Hispanic patients were again found to have a significantly lower likelihood of having guideline concordant follow-up compared to white non-Hispanics

Table 4: Comparison in characteristics of patients with nodules 7mm or greater receiving guideline concordant and non-concordant pulmonary nodule follow-up. Differences found to be statistically significant at a significance value of 0.05 are highlighted in bold.

Patient characteristic	**Guideline concordant (n=230)**	**Guideline non-concordant (n=167)**	**p-value**
Age at scan [mean (SD)]	61.6 (13.4)	62.0 (16.1)	0.82
Male gender	106 (46.1%)	66 (39.5%)	0.19
Ethnicity			0.12
Black non-Hispanic	90 (39.8%)	70 (43.2%)	
White non-Hispanic	97 (42.9%)	59 (36.4%)	
Hispanic/Latino	18 (8.0%)	23 (14.2%)	
Other	21 (9.3%)	10 (6.2%)	
English as primary language	169 (73.5%)	119 (71.7%)	0.69
Insurance			0.60
Medicare	91 (39.6%)	58 (34.9%)	
Medicaid	77 (33.5%)	68 (34.9%)	
Private	46 (20.0%)	33 (19.9%)	
Uninsured	16 (7.0%)	17 (10.2%)	
Current or former smoker	143 (62.2%)	96 (57.5%)	0.35
Marital Status			0.94
Single	83 (36.1%)	63 (37.7%)	
Married	83 (36.1%)	59 (35.3%)	
Other	64 (27.8%)	45 (27.0%)	
Education			0.22
8^{th} grade or less	141(18.7%)	28 (18.4%)	
High School	143 (65.3%)	89 (58.6%)	
College/professional degree	35 (16.0%)	35 (23.0%)	
BMI [mean (SD)]	28.4 (7.0)	28.4 (7.0)	0.95
Income [median (IQR)]	$60,071 ($28,056)	$55,795 ($29,510)	0.07
History of COPD	**68 (29.6%)**	**23 (13.8%)**	**<0.01**
History of diabetes	64 (27.8%)	37 (22.2%)	0.20
History of renal disease	27 (11.7%)	13 (7.8%)	0.20

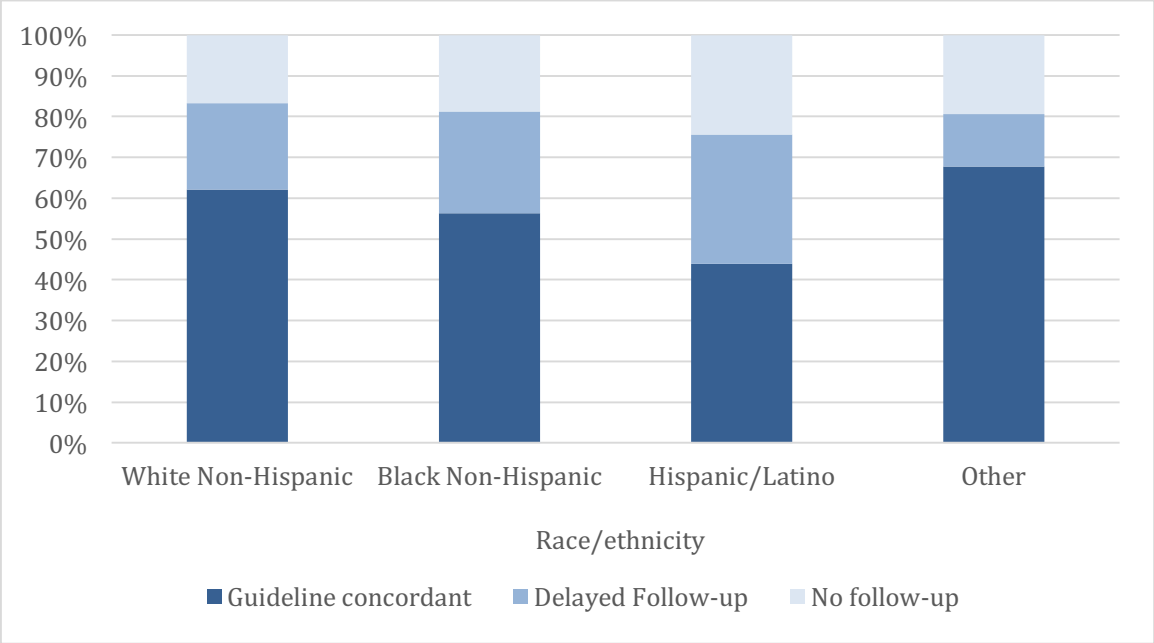
(OR 0.42, CI 0.18–0.99) and patients with COPD had significantly higher odds of having guideline concordant care compared to those without (OR 2.71, CI 1.47–4.99). Uninsured patients had 0.41 times the odds of having guideline concordant follow-up compared to Medicare patients, although this did not reach statistical significance with a p-value of 0.09. Similar patterns were again noted among patients with nodules measuring 7mm or greater who had any follow-up during the study period (Figure 5).

Table 5: Multivariable logistic regression analysis comparing patients with guideline concordant follow-up to guideline non-concordant follow-up for nodules 7mm or greater. Characteristics reaching statistical significance highlighted in bold.

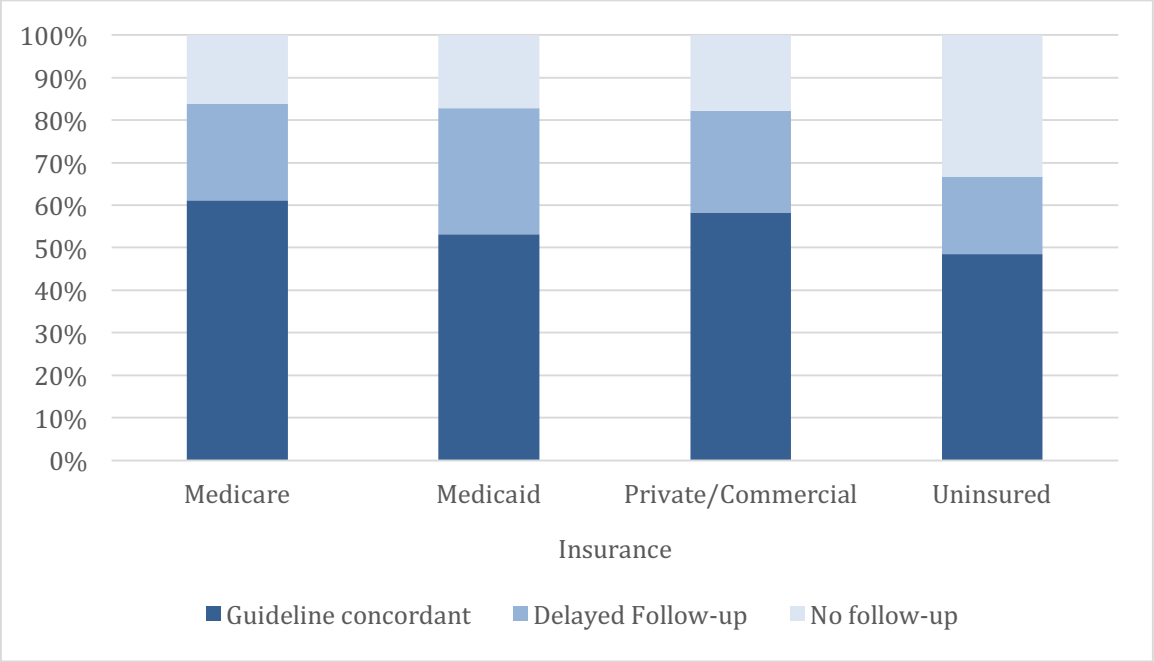
Patient characteristic	Odds ratio (95% CI)	p-value
Race/Ethnicity		
White Non-Hispanic	Ref	
Black Non-Hispanic	0.86 (0.49–1.50)	0.59
Hispanic	**0.42 (0.18–0.99)**	**0.05**
Other	1.50 (0.50–4.54)	0.47
Insurance		
Medicare	Ref	
Medicaid	0.71 (0.39–1.31)	0.27
Commercial/Private	0.90 (0.47–1.71)	0.74
Uninsured	0.41 (0.15–1.16)	0.09
COPD	**2.71 (1.47–4.99)**	**<0.01**

Figure 5: Rates of guideline concordant follow-up, delayed follow-up, and no follow-up for patients with nodules of 7mm or greater based on (a) patient race/ethnicity, and (b) patient insurance status.

a)



b)



DISCUSSION

This study explored the proportion of patients with newly detected incidental pulmonary nodules who received appropriate pulmonary nodule follow-up at BMC based upon 2005 Fleischner Society guidelines. While overall there was a low proportion of guideline-concordant follow-up (53.2%), this is consistent with prior studies that have assessed pulmonary nodule guideline implementation.[59–61] In my study, the rate of concordance only included follow-up at least as aggressive as the guidelines recommend. The actual concordance rate likely would be significantly lower if taking into consideration imaging studies occurring earlier than recommended, given over-evaluation may occur in up to 28% of cases.[60,106] Early evaluation was not included in this study given the inability to determine whether a subsequent CT scan was obtained for a different clinical reason. In these cases, the study may have been intended to evaluate a different disease (such as a pulmonary embolism or pneumonia), but the nodule could also be reassessed at this earlier interval. Additionally, any follow-up chest CT was considered a potential follow-up study without knowledge of the clinical indication for the study. It is likely that a significant number of follow-up studies were obtained for a different clinical purpose and that "nodule follow-up" occurred merely incidentally. For these reasons, it would seem the guideline concordant follow-up rate obtained in this study likely represents the best-case scenario and that the actual rate of guideline concordance is considerably less.

While confirming the low penetration of guideline-recommended pulmonary nodule care into clinical practice, this study also identified potential barriers to guideline concordant pulmonary nodule care. Smaller nodules had higher rates of delayed and absent follow-up, with higher rates of guideline concordance as nodule size increased. This may be due, in part, to clinicians and patients appropriately having greater concern for larger nodules and thus having closer and more reliable follow-up. In other words, this pattern may simply represent greater concern, as opposed to a greater likelihood of being in accordance with guidelines. Prior studies have found mixed results for how nodule size is associated with guideline-recommended follow-up. While one study found no difference in guideline adherence based on nodule size,[61] another found adherence was highest for nodules measuring 4–6mm and decreased as nodule size increased or decreased.[107] My study findings differ from these prior studies, with nodule size being having a strong and graded association with guideline concordance. In cases where the risks of malignancy are highest, clinicians and patients are potentially more likely to follow recommendations given increased concern about a potentially life-threatening diagnosis. Nonetheless, even for nodules measuring 7mm or greater, overall guideline concordance increased to only 57.9%. While larger nodules did have a greater rate of guideline concordant follow-up, there remained a significant number of patients receiving delayed or absent follow-up even for these higher risk nodules.

This study found Hispanic patients to have 0.59 times the odds of having guideline

concordant follow-up compared to white non-Hispanic patients. What was most interesting about this finding was that the association was significant even when controlling for language, education, and income. There appears to be some barrier unique to Hispanics, given there was no similar finding in other minority groups. With language and socioeconomic factors not playing a significant role, one must consider whether there are inherent cultural issues that impede Hispanic patients from receiving guideline-concordant care.[92,93] This finding is not unique to pulmonary nodule management, as Hispanic patients have been found to have lower rates of guideline concordant care in many other conditions: liver disease,[108,109] breast cancer diagnosis and treatment,[110,111] and preventive care[112] among many others. In one attempt to identify an explanation for these disparities in care, Colen *et al.* evaluated the role of acute and chronic discrimination in the health gap between different races and ethnicities.[113] Interestingly, while this study found exposure to unfair treatment explained a significant of disparity in the care of black patients, there was no such association with disparity in care for Hispanics.[113] While the cause for disparities among Hispanics is multifactorial, several qualitative studies in other medical conditions shed potential light on why Hispanics often receive sub-optimal care.[114–116] While these studies involve different medical conditions, there are some common themes that arise as potential barriers for Hispanic patients. For instance, patients across these studies report low health literacy, with difficulty understanding how and why medical tests and procedures need to be performed.[114,115] Additionally, patients are concerned about how

a medical diagnosis might affect not only their own well-being, but the well-being of their family.[116] Finally, there are several comments that reflect a lack of perceived social support among patients.[114–116] Any or all of these factors may potentially explain why Hispanics in my study received less guideline concordant care compared to non-Hispanics.

There were also significantly lower rates of guideline concordance in patients who were uninsured. This may be primarily due to lack of adequate healthcare access and inability of patients to pay for follow-up tests out-of-pocket. Several studies have documented lower rates of healthcare utilization, particularly in preventive care, for patients that are uninsured.[117–119] There are other potential contributing factors for why uninsured patients may receive suboptimal care. Uninsured patients often have low health literacy and increased difficulty with navigating the healthcare system.[120] Additionally, even when uninsured patients have healthcare access, this access may be inadequate for all their health needs. Given that uninsured patients have higher prevalence of comorbidities,[121] there may be need to prioritize health conditions due to limited time or financial resources. For instance, follow-up of a pulmonary nodule may be delayed or even ignored in order to first manage poorly controlled diabetes, congestive heart failure, or significant mental illness. In such cases, it may even be justifiable to not follow pulmonary nodule guidelines and individualize the follow-up plan based on that specific patient's needs.

The strongest association with guideline concordant follow-up in this study was a co-diagnosis of COPD. The diagnosis of a pulmonary nodule in a patient with COPD often presents an interesting conundrum. On the one hand, patients with COPD are at higher risk of having lung cancer, suggesting an identified nodule has greater likelihood of being malignant than in patients without COPD.[122,123] On the other hand, patients with COPD have increased risk of complications related to the diagnostic evaluation of pulmonary nodules or potentially curative lung resection.[70,71,124] My study found patients with COPD to have twice the odds of having guideline concordant pulmonary nodule follow-up compared to those without COPD. One potential explanation would be that patients and their clinicians in this study were more concerned with the risks of malignancy and less about potential complications, given the most common follow-up in this study was non-invasive CT imaging. Another potential explanation is that patients with COPD have closer follow-up than those without COPD, thereby having more exposure to the healthcare system and more opportunity for follow-up. However, arguing against this is the fact that neither diabetes nor chronic kidney disease (two chronic conditions that require frequent follow-up) were associated with guideline concordant care. A final, and perhaps most likely, explanation for this association is the role of pulmonary specialists in the care of COPD patients. COPD patients are more likely to have a pulmonologist following their respiratory disease who may concurrently also follow their pulmonary nodule. It is possible that having a pulmonary specialist managing pulmonary nodule follow-up was an unmeasured confounder that could be

linked to better guideline concordance. This may be due to better familiarity with pulmonary nodule guidelines and more experience with the intricacies of nodule management.[125] Additionally, pulmonologists are more likely than other clinicians to refer directly to the guidelines as opposed to relying on recommendations given by radiologists in the imaging report.[98] However, several prior studies have documented that even pulmonary specialists often do not follow pulmonary nodule guidelines perhaps due to low faith in the quality of evidence upon which they are based.[59,126] Given it could not be determined from the available data which patients had a pulmonologist and which did not, additional data and analysis is needed to better investigate this association.

While this study identified several patient characteristics associated with delayed or absent pulmonary nodule follow-up, there remain multiple other factors impeding implementation of guideline-recommended pulmonary nodule practices. At the onset of this study, the initial plan was to utilize a radiology database tracking all new diagnoses of pulmonary nodules. This was a clinical database that was maintained as part of a quality improvement initiative at BMC. However, close analysis of the database found it unusable for this study given frequent errors in the recording of nodule size or in the diagnosis of a pulmonary nodule itself. In several cases, nodule size was recorded up to 10–15mm different from its actual measurement. This clinical database had been used to track pulmonary nodules and to flag clinicians ordering the initial study about the

need for follow-up. These numerous errors could increase the risk of both under- and over-evaluation of pulmonary nodules by alerting physicians to a nodule of the wrong size and with an inaccurate recommendation for follow-up. In these cases, even if all other factors were optimized and both patient and clinician sought to adhere to guideline-recommended follow-up, patients would still not be receiving the recommended follow-up evaluation. What is perhaps most concerning is that this occurred in a dedicated quality improvement project at a major academic safety net hospital. If nodule evaluation cannot be optimized in this setting with minimal disparities in healthcare delivery, one would expect other institutions that do not have the same pulmonary nodule expertise or focus on at-risk populations would have even more challenges and worse outcomes.

The database errors as well as patient characteristics associated with guideline non-concordance exemplify the complexities involved in patients receiving the recommended pulmonary nodule follow-up. The interrelationships between patient and clinician, patient and healthcare system, and clinician and healthcare system as outlined in my conceptual model are all critical to performing guideline recommended evaluation in practice. An obstacle in any of these relationships (exemplified by the database entry errors identified in my study) can fracture the path towards guideline concordant care. So how do we optimize these paths and improve pulmonary nodule guideline concordance and outcomes? My study highlights several areas in nodule management

that could be potential targets for intervention. First, it is essential to recognize the need to dedicate resources to pulmonary nodule follow-up and to develop a streamlined process for nodule evaluation. The database issues found during this study were not unique to this institution. In fact, many institutions lack the resources and infrastructure needed to facilitate pulmonary nodule evaluation and prevent loss of follow-up.[97] Complicating this further is the role of several medical disciplines in the pulmonary nodule follow-up process, as this may involve the ordering provider (any specialty), radiology, surgeons, pulmonologists, primary care physicians, and oncologists. While results of dedicated nodule clinics have been somewhat mixed,[59] there have been successful implementation of similar clinics in other specialties, such as thyroid nodules.[127] There are multiple benefits to these specialty clinics, including a clear identification of clinician ownership of pulmonary nodule management, expertise in navigating nuances of follow-up, and pooling of resources to assure the necessary infrastructure and processes are in place. However, this type of specialization is not always possible, particularly in more remote settings where resources and healthcare access are more limited.

Another area for investigation is in regards to the guideline recommendations themselves. Nearly half of patients with a nodule measuring 6mm or less in this study received the appropriate follow-up according to the 2005 Fleischner Society guidelines. However, it is unclear based upon the evidence if and when nodules of this size even

need to be followed. Perhaps the guideline concordant follow-up rate for nodules this small is so low due to clinicians' attitude towards the low quality of evidence for this recommendation. In a recent study, nearly 90% of clinicians reported willingness to enroll patients in a clinical trial comparing current guideline recommendations for low risk nodules to less frequent surveillance strategies.[126] In fact, the Fleischner Society recently released updated guidelines recommending no follow-up for low-risk patients with nodules up to 6mm and optional follow-up for high-risk patients with nodules up to 6mm.[128] So while half of patients with nodules of this size in my study received delayed or absent follow-up according to the 2005 guidelines, it is unclear what, if any, impact this may have on their overall outcomes. Similarly, there is discrepancy amongst guidelines themselves about how and when nodules should be evaluated. The American College of Chest Physicians, British Thoracic Society, and Fleischner Guidelines, for instance, all have similar but different recommendations and algorithms for follow-up.[19,56,64,128] With guidelines themselves not in agreement, it is challenging for clinicians and patients to determine the best approach and time period for follow-up. In order to clarify guidelines and better delineate which patients benefit from close follow-up and for which less aggressive follow-up is preferred, further studies are needed to assess patient-oriented outcomes at various nodule follow-up intervals. In fact, the Patient-Centered Outcomes Research Institute recently funded a multi-million dollar, multi-center trial investigating various intervals of follow-up is currently ongoing, with BMC being a participating state.[129]

A final area of potential intervention is at the patient level. In this study, while Hispanic patients and uninsured patients had lower rates of guideline concordant follow-up, non-Hispanics and insured patients still had overall low rates of guideline concordant follow-up. Improving the disparity in care is not sufficient on its own to optimize overall patient outcomes in pulmonary nodule management. However, there are potential lessons that can be learned from these groups with lower rates of follow-up. Uninsured and Hispanic patients both have been found to have low rates of health literacy and difficulty interacting with the healthcare system.[114,120] With pulmonary nodules, however, these traits are not necessarily unique to these groups. Prior studies have found patients have difficulty understanding the diagnosis of a pulmonary nodule in part due to poor communication from healthcare providers.[72,73,104] Pulmonary nodule guidelines from the American College of Chest Physicians recommend shared decision-making in order for patient preferences to play a critical role in the decision-making process.[64,130] While the complexity and uncertainty surrounding pulmonary nodule evaluation can make it challenging to communicate with patients and engage them in the decision-making process, these are the ideal moments for implementing shared decision-making discussions.[131] Multiple studies have found that including patients in the decision-making process can improve their overall satisfaction with their care as well as adherence to medical recommendations.[71–73,132] Better engagement of patients in discussing the diagnosis of a pulmonary nodule and utilization of shared decision-making to determine the optimal plan for follow-up evaluation may be one potential

way to improve patient adherence to recommendations and rates of guideline concordant follow-up.

This study has limitations. Any CT imaging study occurring after the initial pulmonary nodule diagnosis was considered a potential follow-up study, but the reason for obtaining the study could not be ascertained. As such, some follow-up studies may have not been actually intended to be follow-up. This would potentially make the guideline concordant follow-up rates lower than that found in this study. While steps were taken to ensure patients in this study had their primary medical care at BMC, it is possible that some patients may have had follow-up imaging or evaluation at another institution after the initial diagnosis that we could not capture. However, by including only patients with a primary care or pulmonary clinic visit within a year before or after diagnosis, the frequency of patients having follow-up at another institution was likely low. Finally, while this study evaluated patient characteristics associated with guideline concordant follow-up, reasons for delayed or absent follow-up could not be obtained from the dataset. Patient preference or competing clinical conditions with higher acuity could be potentially appropriate reasons for not following guideline recommendations, neither of which could be captured in this study.

While this study found some potential sources for why pulmonary nodule guidelines are infrequently followed in practice, further research is needed to better understand

barriers and how they are best overcome. Additional data collection and analysis is needed to further explore the association of COPD diagnosis with guideline concordance, with particular attention to how having a pulmonary specialist influences follow-up rates. Additional analysis would also aim to assess whether amount of healthcare utilization is associated with nodule follow-up, evaluating how number of clinic visits within the study period may be associated with guideline concordance. Finally, implementation studies are needed to explore strategies for improving workflow and streamlining the process of identifying nodules in higher risk patients, communicating the need for follow-up to patient and clinician, scheduling the recommended follow-up, and ensuring follow-up is completed in a timely manner. These initial next steps will further the understanding of how pulmonary nodule guideline concordance can be improved to optimize follow-up and overall patient outcomes.

CONCLUSION

Overall, the rate of guideline concordant pulmonary nodule follow-up was found to be low. Poor healthcare access (uninsured) and cultural factors (Hispanics) were significant contributors to delayed pulmonary nodule follow-up. Additionally, patients at higher risk of malignancy (larger nodules, co-diagnosis of COPD), had higher likelihood of guideline concordant follow-up. While these patient characteristics provide some explanation for low rates of follow-up, additional factors at the patient, clinician, and healthcare system level also likely contribute to the difficulty with implementing guidelines into clinical practice. Future work is needed to assess how the complex patient-clinician, patient-healthcare system, and clinician-healthcare system dynamics may influence timely pulmonary nodule evaluation.

References

1. Siegel R, Ma J, Zou Z, Jemal A. Cancer statistics, 2014. *CA: A Cancer Journal for Clinicians.* 2014;64(1):9–29.

2. McDaniel AM. Smoking cessation strategies may increase quit rates among adults of low socioeconomic status. *Evidence-Based Nursing.* 2016;19(1):17.

3. Nayan S, Gupta MK, Sommer DD. Evaluating smoking cessation interventions and cessation rates in cancer patients: a systematic review and meta-analysis. *ISRN Oncology.* 2011;2011:849023.

4. Messer K, Trinidad DR, Al-Delaimy WK, Pierce JP. Smoking cessation rates in the United States: a comparison of young adult and older smokers. *American Journal of Public Health.* 2008;98(2):317–322.

5. Hagerman CJ, Tomko CA, Stanton CA, et al. Incorporating a Smoking Cessation Intervention into Lung Cancer Screening Programs: Preliminary Studies. *Journal of Psychosocial Oncology.* 2015;33(6):703–723.

6. Roach MC, Rehman S, DeWees TA, Abraham CD, Bradley JD, Robinson CG. It's never too late: Smoking cessation after stereotactic body radiation therapy for non-small cell lung carcinoma improves overall survival. *Practical Radiation Oncology.* 2016;6(1):12–18.

7. Tanner NT, Kanodra NM, Gebregziabher M, et al. The Association Between Smoking Abstinence and Mortality in the National Lung Screening Trial. *American Journal of Respiratory and Critical Care Medicine.* 2016;193(5):534–541.

8. Slatore CG, Baumann C, Pappas M, Humphrey LL. Smoking behaviors among patients receiving computed tomography for lung cancer screening. Systematic review in support of the U.S. preventive services task force. *Annals of the American Thoracic Society.* 2014;11(4):619–627.

9. Pinsky PF, Gierada DS, Black W, et al. Performance of Lung-RADS in the National Lung Screening Trial: a retrospective assessment. *Annals of Internal Medicine.* 2015;162(7):485–491.

10. McKee BJ, Regis SM, McKee AB, Flacke S, Wald C. Performance of ACR Lung-RADS in a clinical CT lung screening program. *Journal of the American College of Radiology.* 2015;12(3):273–276.

11. Moyer VA, Force USPST. Screening for lung cancer: U.S. Preventive Services Task Force recommendation statement. *Annals of Internal Medicine.* 2014;160(5): 330–338.

12. Wender R, Fontham ET, Barrera E, Jr., et al. American Cancer Society lung cancer screening guidelines. *CA: A Cancer Journal for Clinicians.* 2013;63(2):107–117.

13. Detterbeck FC, Mazzone PJ, Naidich DP, Bach PB. Screening for lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest.* 2013;143(5 Suppl):e78S–92S.

14. Jaklitsch MT, Jacobson FL, Austin JH, et al. The American Association for Thoracic Surgery guidelines for lung cancer screening using low-dose computed tomography scans for lung cancer survivors and other high-risk groups. *Journal of Thoracic and Cardiovascular Surgery.* 2012;144(1):33–38.

15. National Lung Screening Trial Research T, Aberle DR, Adams AM, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. *New England Journal of Medicine.* 2011;365(5):395–409.

16. Montani F, Marzi MJ, Dezi F, et al. miR-Test: a blood test for lung cancer early detection. *Journal of the National Cancer Institute.* 2015;107(6):djv063.

17. Wozniak MB, Scelo G, Muller DC, Mukeria A, Zaridze D, Brennan P. Circulating MicroRNAs as Non-Invasive Biomarkers for Early Detection of Non-Small-Cell Lung Cancer. *PLoS One.* 2015;10(5):e0125026.

18. Wiener RS, Gould MK, Arenberg DA, et al. An official American Thoracic Society/American College of Chest Physicians policy statement: implementation of low-dose computed tomography lung cancer screening programs in clinical practice. *American Journa of Respiratory and Critical Care Medicine.* 2015; 192(7):881–891.

19. Baldwin DR, Callister ME, Guideline Development G. The British Thoracic Society guidelines on the investigation and management of pulmonary nodules. *Thorax.* 2015;70(8):794–798.

20. Basch E, Oliver TK, Vickers A, et al. Screening for prostate cancer with prostate-specific antigen testing: American Society of Clinical Oncology Provisional Clinical Opinion. *Journal of Clinical Oncology.* 2012;30(24):3020–3025.

21. Drazer MW, Prasad SM, Huo D, et al. National trends in prostate cancer screening among older American men with limited 9-year life expectancies: evidence of an increased need for shared decision making. *Cancer.* 2014;120(10): 1491–1498.

22. Moyer VA, Force USPST. Screening for prostate cancer: U.S. Preventive Services Task Force recommendation statement. *Annals of Internal Medicine.* 2012; 157(2):120–134.

23. Schroder FH, Hugosson J, Roobol MJ, et al. Screening and prostate-cancer mortality in a randomized European study. *New England Journal of Medicine.* 2009;360(13):1320–1328.

24. Graham EAaS, J.J. Three Cases of Resection of Calcifed Pulmonary Abscess (or Tuberculosis) Stimulating Tumor. *Journal of Thoracic Surgery.* 1936;173(6).

25. Harrington SW. The surgical treatment of circumscribed intrathoracic lesions; lesions found on routine thoracic roentgenologic examination, with absence of subjective symptoms. *Dis Chest.* 1951;19(3):255–270.

26. Alexander J. Circumscribed Intrathoracic Neoplasma. *The Journal of the American Medical Association.* 1942;195:395.

27. Webb WA, Thoroughman JC. Solitary pulmonary nodule due to Brucella suis. Report of a case. *Diseases of the Chest.* 1966;49(2):222–224.

28. Rosen VJ, Christiansen TW, Hughes RK. Metastatic thymoma presenting as a solitary pulmonary nodule. *Cancer.* 1966;19(4):527–532.

29. Keresteci AG, Mitchell RI. Squamous cell carcinoma of the kidney presenting as a solitary pulmonary nodule. *Canadian Journal of Surgery.* 1966;9(2):176–180.

30. Chrisholm JC, Lang GR. Solitary circumscribed pulmonary nodule. An unusual manifestation of sarcoidosis. *Archives of Internal Medicine.* 1966;118(4):376–378.

31. Fadhli H, Derrick JR. Twisted lingula. A cause of a solitary pulmonary nodule. *Annals of Thoracic Surgery.* 1965;1(6):753–754.

32. Osborne DP, Brown RB, Dimmette RM. Solitary pulmonary nodule due to Ascaris lumbricoides. *Diseases of the Chest.* 1961;40:308–310.

33. Good CA, Wilson TW. The solitary circumscribed pulmonary nodule; study of seven hundred five cases encountered roentgenologically in a period of three and one-half years. *Journal of the American Medical Association.* 1958;166(3): 210–215.

34. Davis EW, Katz S, Peabody JW, Jr. The solitary pulmonary nodule; a ten year study based on 215 cases. *Journal of Thoracic Surgery.* 1956;32(6):728–770; discussion, 770–721.

35. Ayers WR, Huang HK. The use of computerized tomography in the diagnosis of pulmonary nodules. *Computerized Tomography.* 1978;2(2):55–62.

36. Muhm JR, Brown LR, Crowe JK. Detection of pulmonary nodules by computed tomography. *AJR American Journal of Roentgenology.* 1977;128(2):267–270.

37. Shin MS, Ho KJ. Computed tomographic evaluation of solitary pulmonary nodules in chest roentgenograms. *Journal of Computer Assisted Tomography.* 1982;6(5):947–954.

38. Cann CE, Gamsu G, Birnberg FA, Webb WR. Quantification of calcium in solitary pulmonary nodules using single- and dual-energy CT. *Radiology.* 1982;145(2): 493–496.

39. Muhm JR. Solitary pulmonary nodule: evaluation by tomography. *Geriatrics.* 1982;37(10):125–127, 131.

40. Godwin JD, Speckman JM, Fram EK, et al. Distinguishing benign from malignant pulmonary nodules by computed tomography. *Radiology.* 1982;144(2):349–351.

41. Hall WB, Truitt SG, Scheunemann LP, et al. The prevalence of clinically relevant incidental findings on chest computed tomographic angiograms ordered to diagnose pulmonary embolism. *Archives of Internal Medicine.* 2009;169(21): 1961–1965.

42. Rinaldi MF, Bartalena T, Giannelli G, et al. Incidental lung nodules on CT examinations of the abdomen: prevalence and reporting rates in the PACS era. *European Journal of Radiology.* 2010;74(3):e84–88.

43. Gould MK, Tang T, Liu IL, et al. Recent Trends in the Identification of Incidental Pulmonary Nodules. *American Journal of Respiratory and Critical Care Medicine.* 2015;192(10):1208–1214.

44. Swensen SJ, Silverstein MD, Ilstrup DM, Schleck CD, Edell ES. The probability of malignancy in solitary pulmonary nodules. Application to small radiologically indeterminate nodules. *Archives of Internal Medicine.* 1997;157(8):849–855.

45. Aoki T, Nakata H, Watanabe H, et al. Evolution of peripheral lung adenocarcinomas: CT findings correlated with histology and tumor doubling time. *AJR American Journal of Roentgenology.* 2000;174(3):763–768.

46. Hasegawa M, Sone S, Takashima S, et al. Growth rate of small lung cancers detected on mass CT screening. *British Journal of Radiology.* 2000;73(876):1252–1259.

47. Kostis WJ, Yankelevitz DF, Reeves AP, Fluture SC, Henschke CI. Small pulmonary nodules: reproducibility of three-dimensional volumetric measurement and estimation of time to follow-up CT. *Radiology.* 2004;231(2):446–452.

48. Usuda K, Saito Y, Sagawa M, et al. Tumor doubling time and prognostic assessment of patients with primary lung cancer. *Cancer.* 1994;74(8):2239–2244.

49. Winer-Muram HT, Jennings SG, Tarver RD, et al. Volumetric growth rate of stage I lung cancer prior to treatment: serial CT scanning. *Radiology.* 2002;223(3):798–805.

50. Henschke CI, McCauley DI, Yankelevitz DF, et al. Early Lung Cancer Action Project: overall design and findings from baseline screening. *Lancet.* 1999; 354(9173):99–105.

51. Henschke CI, Yankelevitz DF, Naidich DP, et al. CT screening for lung cancer: suspiciousness of nodules according to size on baseline scans. *Radiology.* 2004; 231(1):164–168.

52. Benjamin MS, Drucker EA, McLoud TC, Shepard JA. Small pulmonary nodules: detection at chest CT and outcome. *Radiology.* 2003;226(2):489–493.

53. U.S. Department of Health and Human Services. The health consequences of smoking: a report of the surgeon general. *US Department of Health and Human Services, Center for Disease Control and Prevention.* 1982.

54. Lee PN. Relation between exposure to asbestos and smoking jointly and the risk of lung cancer. *Occupational and Environmental Medicine.* 2001;58(3):145–153.

55. Mayne ST, Buenconsejo J, Janerich DT. Familial cancer history and lung cancer risk in United States nonsmoking men and women. *Cancer Epidemiology, Biomarkers and Prevention.* 1999;8(12):1065–1069.

56. MacMahon H, Austin JH, Gamsu G, et al. Guidelines for management of small pulmonary nodules detected on CT scans: a statement from the Fleischner Society. *Radiology.* 2005;237(2):395–400.

57. Albert RH, Russell JJ. Evaluation of the solitary pulmonary nodule. *American Family Physician.* 2009;80(8):827–831.

58. Tan BB, Flaherty KR, Kazerooni EA, Iannettoni MD, American College of Chest P. The solitary pulmonary nodule. *Chest.* 2003;123(1 Suppl):89S–96S.

59. Veeramachaneni NK, Crabtree TD, Kreisel D, et al. A thoracic surgery clinic dedicated to indeterminate pulmonary nodules: too many scans and too little pathology? *Journal of Thoracic and Cardiovascular Surgery.* 2009;137(1):30–35.

60. Wiener RS, Gould MK, Slatore CG, Fincke BG, Schwartz LM, Woloshin S. Resource use and guideline concordance in evaluation of pulmonary nodules for cancer: too much and too little care. *JAMA Internal Medicine.* 2014;174(6):871–880.

61. Ridge CA, Hobbs BD, Bukoye BA, et al. Incidentally detected lung nodules: clinical predictors of adherence to Fleischner Society surveillance guidelines. *Journal of Computer Assisted Tomography.* 2014;38(1):89–95.

62. Eisenberg RL, Bankier AA, Boiselle PM. Compliance with Fleischner Society guidelines for management of small lung nodules: A survey of 834 radiologists. *Radiology.* 2010;255(1):218–224.

63. Esmaili A, Munden RF, Mohammed TL. Small pulmonary nodule management: a survey of the members of the Society of Thoracic Radiology with comparison to the Fleischner Society guidelines. *Journal of Thoracic Imaging.* 2011;26(1):27–31.

64. Gould MK, Donington J, Lynch WR, et al. Evaluation of individuals with pulmonary nodules: when is it lung cancer? Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest.* 2013;143(5 Suppl):e93S–120S.

65. Tanner NT, Aggarwal J, Gould MK, et al. Management of Pulmonary Nodules by Community Pulmonologists: A Multicenter Observational Study. *Chest.* 2015; 148(6):1405–1414.

66. Tanner NT, Porter A, Gould M, Li XJ, Vachani A, Silvestri GA. Physician assessment of pre-test probability of malignancy and adherence with guidelines for pulmonary nodule evaluation. *Chest.* 2017;152(2):263–270.

67. Reich J. Stage IA lung cancer size and survival. *Chest.* 2004;126(1):310–311; author reply 311.

68. Birim O, Kappetein AP, Takkenberg JJ, van Klaveren RJ, Bogers AJ. Survival after pathological stage IA nonsmall cell lung cancer: tumor size matters. *Annals of Thoracic Surgery.* 2005;79(4):1137–1141.

69. Wang T, Nelson RA, Bogardus A, Grannis FW, Jr. Five-year lung cancer survival: which advanced stage nonsmall cell lung cancer patients attain long-term survival? *Cancer.* 2010;116(6):1518–1525.

70. Wiener RS, Schwartz LM, Woloshin S, Welch HG. Population-based risk for complications after transthoracic needle lung biopsy of a pulmonary nodule: an analysis of discharge records. *Annals of Internal Medicine.* 2011;155(3):137–144.

71. Wiener RS, Wiener DC, Gould MK. Risks of Transthoracic Needle Biopsy: How High? *Clinical Pulmonary Medicine.* 2013;20(1):29–35.

72. Slatore CG, Press N, Au DH, Curtis JR, Wiener RS, Ganzini L. What the heck is a "nodule"? A qualitative study of veterans with pulmonary nodules. *Annals of the American Thoracic Society.* 2013;10(4):330–335.

73. Wiener RS, Gould MK, Woloshin S, Schwartz LM, Clark JA. 'The thing is not knowing': patients' perspectives on surveillance of an indeterminate pulmonary nodule. *Health Expectations.* 2015;18(3):355–365.

74. Slatore CG, Wiener RS, Golden SE, Au DH, Ganzini L. Longitudinal Assessment of Distress among Veterans with Incidental Pulmonary Nodules. *Annals of the American Thoracic Society.* 2016;13(11):1983–1991.

75. Barnett PG, Ananth L, Gould MK, Veterans Affairs Positron Emission Tomography Imaging in the Management of Patients with Solitary Pulmonary Nodules Cooperative Study G. Cost and outcomes of patients with solitary pulmonary nodules managed with PET scans. *Chest.* 2010;137(1):53–59.

76. Kinsinger LS, Anderson C, Kim J, et al. Implementation of Lung Cancer Screening in the Veterans Health Administration. *JAMA Internal Medicine.* 2017;177(3): 399–406.

77. McKee BJ, McKee AB, Flacke S, Lamb CR, Hesketh PJ, Wald C. Initial experience with a free, high-volume, low-dose CT lung cancer screening program. *Journal of the American College of Radiology.* 2013;10(8):586–592.

78. Mazzone P. The rationale for, and design of, a lung cancer screening program. *Cleveland Clinical Journal of Medicine.* 2012;79(5):337–345.

79. Arenberg D, Kazerooni EA. Setting up a lung cancer screening program. *Journal of the National Comprehensive Cancer Network.* 2012;10(2):277–285.

80. Laiteerapong N, Fairchild PC, Chou CH, Chin MH, Huang ES. Revisiting Disparities in Quality of Care Among US Adults With Diabetes in the Era of Individualized Care, NHANES 2007–2010. *Medical Care.* 2015;53(1):25–31.

81. Hasegawa K, Stoll SJ, Ahn J, Kysia RF, Sullivan AF, Camargo CA, Jr. Association of Insurance Status with Severity and Management in ED Patients with Asthma Exacerbation. *Western Journal of Emergency Medicine.* 2016;17(1):22–27.

82. Cram P, Saag KG, Lou Y, et al. Racial Differences and Disparities in Osteoporosis-related Bone Health: Results From the PAADRN Randomized Controlled Trial. *Medical Care.* 2017;55(6):561–568.

83. Richardson KK, Bokhour B, McInnes DK, et al. Racial Disparities in HIV Care Extend to Common Comorbidities: Implications for Implementation of Interventions to Reduce Disparities in HIV Care. *Journal of the National Medical Association.* 2016;108(4):201–210 e203.

84. Hess PL, Hernandez AF, Bhatt DL, et al. Sex and Race/Ethnicity Differences in Implantable Cardioverter-Defibrillator Counseling and Use Among Patients Hospitalized With Heart Failure: Findings from the Get With The Guidelines-Heart Failure Program. *Circulation.* 2016;134(7):517–526.

85. Eapen ZJ, Liang L, Shubrook JH, et al. Current quality of cardiovascular prevention for Million Hearts: an analysis of 147,038 outpatients from The Guideline Advantage. *American Heart Journal.* 2014;168(3):398–404.

86. Tung EL, Baig AA, Huang ES, Laiteerapong N, Chua KP. Racial and Ethnic Disparities in Diabetes Screening Between Asian Americans and Other Adults: BRFSS 2012–2014. *Journal of General Internal Medicine.* 2017;32(4):423–429.

87. Shao Z, Richie WD, Bailey RK. Racial and Ethnic Disparity in Major Depressive Disorder. *Journal of Racial and Ethnic Health Disparities.* 2016;3(4):692–705.

88. Fitzgerald S, Chao J, Feferman Y, Perumalswami P, Sarpel U. Hepatitis B and Hepatocellular Carcinoma Screening Practices in Chinese and African Immigrant-Rich Neighborhoods in New York City. *Journal of Racial and Ethnic Health Disparitie.* 2016.

89. Yang R, Cheung MC, Byrne MM, et al. Do racial or socioeconomic disparities exist in lung cancer treatment? *Cancer.* 2010;116(10):2437–2447.

90. Lathan CS, Neville BA, Earle CC. The effect of race on invasive staging and surgery in non-small-cell lung cancer. *Journal of Clinical Oncology.* 2006;24(3):413–418.

91. Coughlin SS, Matthews-Juarez P, Juarez PD, Melton CE, King M. Opportunities to address lung cancer disparities among African Americans. *Cancer Medicine.* 2014;3(6):1467–1476.

92. Jonnalagadda S, Bergamo C, Lin JJ, et al. Beliefs and attitudes about lung cancer screening among smokers. *Lung Cancer.* 2012;77(3):526–531.

93. Bergamo C, Lin JJ, Smith C, et al. Evaluating beliefs associated with late-stage lung cancer presentation in minorities. *Journal of Thoracic Oncology.* 2013; 8(1):12–18.

94. Hajjaj FM, Salek MS, Basra MK, Finlay AY. Non-clinical influences on clinical decision-making: a major challenge to evidence-based practice. *Journal of the Royal Society of Medicine.* 2010;103(5):178–187.

95. McKinlay JB, Potter DA, Feldman HA. Non-medical influences on medical decision-making. *Social Science & Medicine.* 1996;42(5):769–776.

96. Charles C, Gafni A, Whelan T. Decision-making in the physician-patient encounter: revisiting the shared treatment decision-making model. *Social Sciencee & Medicine.* 1999;49(5):651–661.

97. Simmons J, Gould MK, Iaccarino J, Slatore CG, Wiener RS. Systems-Level Resources for Pulmonary Nodule Evaluation in the United States: A National Survey. *American Journal of Respiratory and Critical Care Medicine.* 2016;193(9): 1063–1065.

98. Golden SE, Wiener RS, Sullivan D, Ganzini L, Slatore CG. Primary Care Providers and a System Problem: A Qualitative Study of Clinicians Caring for Patients With Incidental Pulmonary Nodules. *Chest.* 2015;148(6):1422–1429.

99. Wiener RS, Slatore CG, Gillespie C, Clark JA. Pulmonologists' Reported Use of Guidelines and Shared Decision-making in Evaluation of Pulmonary Nodules: A Qualitative Study. *Chest.* 2015;148(6):1415–1421.

100. Singh H, Hirani K, Kadiyala H, et al. Characteristics and predictors of missed opportunities in lung cancer diagnosis: an electronic health record-based study. *Journal of Clinical Oncology.* 2010;28(20):3307–3315.

101. Schoen MW, Tabak RG, Salas J, Scherrer JF, Buckhold FR. Comparison of Adherence to Guideline-Based Cholesterol Treatment Goals in Men Versus Women. *American Journal of Cardiology.* 2016;117(1):48–*53*.

102. Kim G, Ford KL, Chiriboga DA, Sorkin DH. Racial and ethnic disparities in healthcare use, delayed care, and management of diabetes mellitus in older adults in California. *Journal of the American Geriatrics Society.* 2012;60(12): 2319–2325.

103. Burgess DJ, van Ryn M, Grill J, et al. Presence and correlates of racial disparities in adherence to colorectal cancer screening guidelines. *Journal of General Internal Medicine.* 2011;26(3):251–258.

104. Wiener RS, Gould MK, Woloshin S, Schwartz LM, Clark JA. What do you mean, a spot?: A qualitative analysis of patients' reactions to discussions with their physicians about pulmonary nodules. *Chest.* 2013;143(3):672–677.

105. American Fact Finder: Community Facts. United States Census Bureau. Washington DC. 2011–2015. Accessed at https://factfinder.census.gov/faces/nav/jsf/pages/index.xhtml on 2 July 2017.

106. Masciocchi M, Wagner B, Lloyd B. Quality review: Fleischner criteria adherence by radiologists in a large community hospital. *Journal of the American College of Radiology.* 2012;9(5):336–339.

107. Lacson R, Prevedello LM, Andriole KP, et al. Factors associated with radiologists' adherence to Fleischner Society guidelines for management of pulmonary nodules. *Journal of the American College of Radiology.* 2012;9(7):468–473.

108. Alkhalili E, Greenbaum A, Luo L, et al. Racial disparities in treatment and survival of hepatocellular carcinoma in native Americans and Hispanics. *American Journal of Surgery.* 2017;214(1):100–104.

109. Kim HS, Rotundo L, Yang JD, et al. Racial/ethnic disparities in the prevalence and awareness of Hepatitis B virus infection and immunity in the United States. *Journal of Viral Hepatitis.* 2017. doi: 10.1111/jvh.12735

110. Martinez ME, Gomez SL, Tao L, et al. Contribution of clinical and socioeconomic factors to differences in breast cancer subtype and mortality between Hispanic and non-Hispanic white women. *Breast Cancer Research and Treatment.* 2017. doi: 10.1007/s10549-017-4389-z.

111. Ahmed AT, Welch BT, Brinjikji W, et al. Racial Disparities in Screening Mammography in the United States: A Systematic Review and Meta-analysis. *Journal of the American College of Radiology.* 2017;14(2):157–165 e159.

112. Travers JL, Schroeder KL, Blaylock TE, Stone PW. Racial/Ethnic Disparities in Influenza and Pneumococcal Vaccinations Among Nursing Home Residents: A Systematic Review. *Gerontologist.* 2017. doi: 10.1093/geront/gnw193

113. Colen CG, Ramey DM, Cooksey EC, Williams DR. Racial disparities in health among nonpoor African Americans and Hispanics: The role of acute and chronic discrimination. *Social Science and Medicine.* 2017. pii: S0277-9536(17)30290-3

114. Jacobs RJ, Ownby RL, Acevedo A, Waldrop-Valverde D. A qualitative study examining health literacy and chronic illness self-management in Hispanic and non-Hispanic older adults. *Journal of Multidisciplinary Healthcare.* 2017;10:167–177.

115. Mansyur CL, Rustveld LO, Nash SG, Jibaja-Weiss ML. Social factors and barriers to self-care adherence in Hispanic men and women with diabetes. *Patient Education and Counseling.* 2015;98(6):805–810.

116. Ramos AK, Correa A, Trinidad N. Perspectives on Breast Health Education and Services Among Recent Hispanic Immigrant Women in the Midwest: a Qualitative Study in Lancaster County, Nebraska. *Journal of Cancer Education.* 2016;31(4):666–672.

117. Holden CD, Chen J, Dagher RK. Preventive care utilization among the uninsured by race/ethnicity and income. *American Journal of Preventive Medicine.* 2015; 48(1):13–21.

118. Spain P, Teixeira-Poit S, Halpern MT, et al. The National Cancer Institute Community Cancer Centers Program (NCCCP): Sustaining Quality and Reducing Disparities in Guideline-Concordant Breast and Colon Cancer Care. *Oncologist.* 2017;22(8):910–917.

119. Kenik J, Jean-Jacques M, Feinglass J. Explaining racial and ethnic disparities in cholesterol screening. *Preventive Medicine.* 2014;65:65–69.

120. Lane SD, Huntington SJ, Satterly LB, Rubinstein RA, Keefe RH, Amaus Project Student R. Filling out the forms: Health literacy among the uninsured. *Social Work in Health Care.* 2017:1–14.

121. Akinyemiju T, Jha M, Moore JX, Pisu M. Disparities in the prevalence of comorbidities among US adults by state Medicaid expansion status. *Preventive Medicine.* 2016;88:196–202.

122. Maldonado F, Bartholmai BJ, Swensen SJ, Midthun DE, Decker PA, Jett JR. Are airflow obstruction and radiographic evidence of emphysema risk factors for lung cancer? A nested case-control study using quantitative emphysema analysis. *Chest.* 2010;138(6):1295–1302.

123. de Torres JP, Bastarrika G, Wisnivesky JP, et al. Assessing the relationship between lung cancer risk and emphysema detected on low-dose CT of the chest. *Chest.* 2007;132(6):1932–1938.

124. Takahashi Y, Matsuda M, Aoki S, et al. Qualitative Analysis of Preoperative High-Resolution Computed Tomography: Risk Factors for Pulmonary Complications After Major Lung Resection. *Annals of Thoracic Surgery.* 2016;101(3):1068–1074.

125. Rajupet S, Doshi D, Wisnivesky JP, Lin JJ. Attitudes About Lung Cancer Screening: Primary Care Providers Versus Specialists. *Clinical Lung Cancer.* 2017. pii: S1525-7304(17)30138-9

126. Iaccarino JM, Simmons J, Gould MK, et al. Clinical Equipoise and Shared Decision-making in Pulmonary Nodule Management. A Survey of American Thoracic Society Clinicians. *Annals of the American Thoracic Society.* 2017;14(6):968–975.

127. Migdal AL, Sternberg SB, Oshin A, Aronson MD, Hennessey JV. Building a Quality Management System for a Thyroid Nodule Clinic. *Thyroid.* 2016;26(6):825–830.

128. MacMahon H, Naidich DP, Goo JM, et al. Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017. *Radiology.* 2017;284(1):228–243.

129. Gould MK. Pragmatic trial of more versus less intensive strategies for active surveillance of patients with small pulmonary nodules. 2015. Accessed at http://www.pcori.org/research-results/2015/pragmatic-trial-more-versus-less-intensive-strategies-active-surveillance on 4 August 2016.

130. Ost DE, Gould MK. Decision making in patients with pulmonary nodules. *American Journal of Respiratory and Critical Care Medicine.* 2012;185(4):363–372.

131. Legare F, Ratte S, Gravel K, Graham ID. Barriers and facilitators to implementing shared decision-making in clinical practice: update of a systematic review of health professionals' perceptions. *Patient Education and Counseling.* 2008; 73(3):526–535.

132. Politi MC, Clark MA, Ombao H, Dizon D, Elwyn G. Communicating uncertainty can lead to less decision satisfaction: a necessary cost of involving patients in shared decision making? *Health Expectations.* 2011;14(1):84–91.

CURRICULUM VITAE